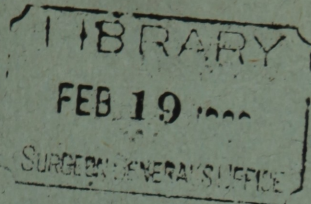


Bloomfield, A.  
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CLINICAL OBSERVATIONS ON EPIDEMIC  
INFLUENZA

By ARTHUR BLOOMFIELD and GEORGE A. HARROP, JR.

(From the Medical Clinic of The Johns Hopkins Hospital)





## CLINICAL OBSERVATIONS ON EPIDEMIC INFLUENZA<sup>1</sup>

By ARTHUR BLOOMFIELD and GEORGE A. HARROP, JR.

(*From the Medical Clinic of The Johns Hopkins Hospital*)

During the recent epidemic of influenza, about 300 cases [1] of the disease were admitted to The Johns Hopkins Hospital. Inasmuch as most of the patients were seen from the very onset of symptoms and went through their illness without complications, an unusual opportunity was afforded to study the clinical features of the entire course of the disease. The material was drawn from certain limited groups of individuals, to wit:

The nursing staff of the hospital (about 350 in number), living in the nurses' home.

The medical students (about 400 in number) quartered in boarding houses and clubs.

The hospital physicians (about 100 in number), residing mainly in the hospital.

The hospital service staff (about 200 in number), living mainly in the domestic home of the hospital or in the nurses' home.

Eight cases arose among the patients in the public wards and a few more were admitted as emergencies from various parts of the city.

Of the entire group, about 300, or approximately 30 per cent, developed the disease; of the nurses, nearly 40 per cent fell ill.

The main statistical facts of the epidemic are summarized in the following table and chart, which are based on the study of 268 patients admitted between September 24th and October 20th.

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<sup>1</sup> Read before The Johns Hopkins Hospital Medical Society, November 18, 1918.

TABLE I

[1] GENERAL STATISTICS OF THE INFLUENZA CASES IN THE JOHNS  
HOPKINS HOSPITAL

	No.	Per Cent
Total cases .....	268	
Total deaths .....	13	4.8
Total number developing pneumonia.....	41	15.3
Total deaths among pneumonia patients.....	13	32.0
Total deaths among patients in hospital from start of disease .....	7	2.7
Total number of patients in hospital from start of disease developing pneumonia.....	28	11.0
Total number of patients admitted with frank pneumonia .....	13	
Total deaths among patients admitted with pneumonia .....	6	46.0
Total deaths among patients developing pneumonia in the hospital.....	7	25.0
Total number of nurses admitted.....	123	
Total number developing pneumonia.....	12	9.8
Total deaths .....	3	2.4
Total deaths of patients developing pneumonia....	3	25.0

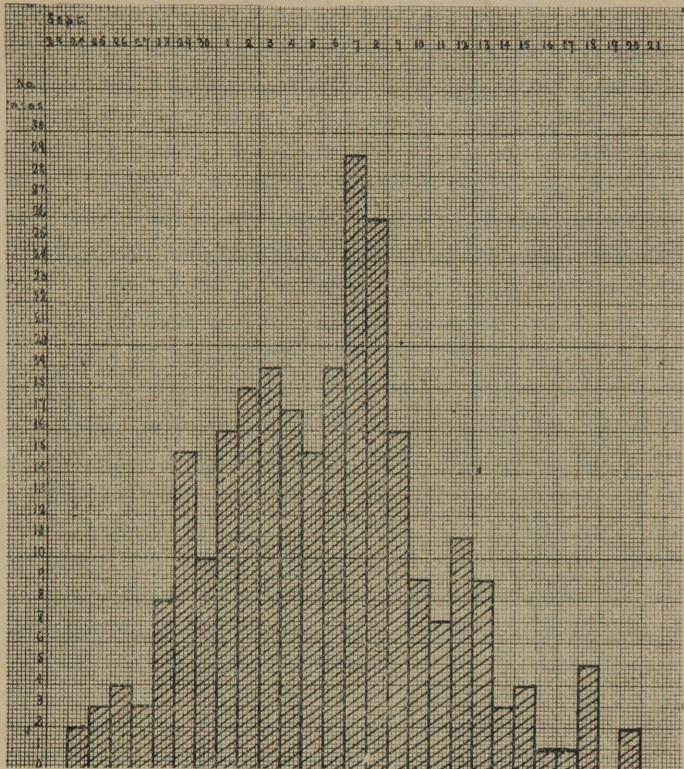
- [2] Chart I illustrates graphically the course of the epidemic. The rapid rise following the few preliminary cases, and the sudden drop after the height of the epidemic was reached, correspond with the curves of previous epidemics. With the sudden falling off in the number of cases there was a remarkable change in the clinical character of the disease. The fulminating type was no longer seen, the patients were much less ill, the erythema of skin and mucous membranes was slight or absent, pneumonia was much less frequent, and in general the picture approximated closely that seen in "influenza nostras," or "endemic grippe." All the patients who died fell ill before October 10th.

The appearance of the epidemic made necessary a rapid reorganization of the hospital, in order to handle the increasing number of cases. This was made possible by the efficient activities of the superintendent's office and of the superintendent of nurses. The disposition of the patients was planned with the idea of preventing secondary epidemics of



pneumonia. Not more than thirty patients were housed in [2] one ward, the rows of beds were single, and screens were placed between every two beds. Each patient had a separate thermometer, and all linen, utensils and dishes were boiled

CHART I



NUMBER OF CASES BY DAY OF ONSET.

after use. Paper towels, handkerchiefs and sputum cups were burned. The patients were instructed to cover the mouth when coughing, and all attendants wore gowns and gauze masks (4 to 8 thicknesses) while in the wards. As soon as pneumonia or any other complication developed, the patient was specially isolated in a separate room.

Each block of twenty to forty cases was in charge of an interne, assisted by one or more fourth-year medical students.



[2] They took the histories, made the notes, carried out the laboratory tests, and had charge of the immediate needs of the patients. The resident and assistant resident exercised systematic supervision over the wards, and the physician-in-chief consulted in the severe cases and advised generally in the conduct of the epidemic. Admission of patients was done by a set of externes rapidly trained in the diagnosis of influenza. Throughout the entire epidemic no case of another infectious disease was admitted to the influenza wards. The organization of the "influenza staff" would have been ideal had it not been necessary constantly to replace men stricken down by the disease. Thus, by the end of the epidemic the entire staff except three members had been renewed by successive substitutes.

It was found necessary to schematize in the handling of the patients, owing to the tremendous nursing problem. A set of routine orders for influenza cases was therefore worked out, which applied automatically to all patients. These orders covering the main needs of most patients were supplemented by any special directions necessary. Another routine was worked out for the regulation of the patients' activity during convalescence. This was found satisfactory in practically all the uncomplicated cases, and saved much labor for the ward staff. No medical or scientific books, or newspapers, were allowed in the wards. It was thought that the harrowing accounts of the epidemic in the latter might have a bad effect on patients already depressed.

The routine study of the case consisted of a history uniformly taken to cover in detail such questions as exposure and onset symptoms, a complete and thorough physical examination, a leucocyte count on admission, and at intervals until discharge, blood pressure on admission and discharge, urine examination on admission, repeated if abnormal findings were present, and two-hourly observations of temperature, pulse and respiration. Frequent detailed notes were made by the internes and staff on the course of the disease and its special features.



## CLINICAL OBSERVATIONS

The material furnished an unusual opportunity to study [2] the early stages of the disease, since about one-half of the cases were drawn from a closed group of individuals—namely, some 350 nurses residing in The Johns Hopkins Nurses' Home. At the start of the epidemic it was hoped that extensive spread among the nursing staff might be prevented by early detection and isolation. Communication between this group and the outside world was, therefore, almost completely cut off, and they came in contact only with each other, with the staff, and with the patients in the wards. Furthermore, they were instructed to report for observation at the first symptom of any sort. Practically all the cases, therefore, were seen from the very start, and it was possible to study in detail the earliest symptoms and the mode of onset. From these observations, it was clearly apparent that the disease is not [3] primarily a local respiratory infection, and that it presents a clean-cut, definite clinical picture, quite independent of pulmonary complications. It should also be emphasized that influenza, as seen now, corresponds in detail with the descriptions of the previous pandemics—it is undoubtedly the same disease.

The disease is ushered in by two groups of symptoms; in the first place the constitutional reactions of an acute febrile disease—headache, general aching, chills, fever, malaise, prostration, anorexia, nausea or vomiting; and in the second place, symptoms referable to an intense congestion of the mucous membranes of the nose, pharynx, larynx, trachea, the upper respiratory tract in general, and of the conjunctivæ. Superficially, the onset seems to vary in different cases, depending on whether one or the other of these sets of symptoms predominates, but a striking essential similarity prevails, which is most obvious during the height of the epidemic, when the disease runs more constantly true to type. For this reason it seems misleading to divide the ordinary run of cases into respiratory, abdominal and nervous. It would seem better to reserve the last term for those patients showing organic lesions of the nervous system or psychoses more outspoken than the usual temporary depressions.

[3] Three distinct types of invasion were noted—abrupt invasion, gradual invasion and invasion with intermittent symptoms. The departure from health was extremely sudden in many of the cases, especially the severe ones at the height of the epidemic, definite symptoms beginning after only a few hours of vague malaise. In some cases the patient was knocked flat, literally dropping in his tracks. The most common symptoms were sudden and marked malaise and prostration, chills or chilly sensations, intense headache and general aching, pain in the eyes and photophobia. In a few instances, acute abdominal pain, vomiting or diarrhea ushered in the disease. In these severe cases the temperature usually rises rapidly, reaching its height within 24 hours. Coincident with, or shortly following onset, as the hyperemia of the mucous membranes develops, there is dryness, tightness, fullness, or slight rawness of the throat, substernal discomfort, and tight, racking cough, without sputum. There may be stoppage of the nose from swelling of the mucous membrane, with slight watery nasal discharge, and conjunctivitis is practically always present. The remarkable flushed appearance of the face and buccal cavity to be described below is usually fully developed in twenty-four hours. In another large group of cases the invasion is gradual, the symptoms unfolding themselves over a period of one to three days before the disease becomes full blown. It is in this group that isolated symptoms, such as headache, sore eyes, "coryza," raw throat, dry cough, anorexia, insomnia, or pain in the back may for a time predominate, masking at first the essential identity of all the cases. During such a period of invasion the temperature is usually normal, or only slightly elevated. In the early part of the epidemic, we observed many cases of this sort for two or three days, uncertain as to the diagnosis, until sudden high fever and frank symptoms and signs made the condition obvious. In a third group of cases the early symptoms were very puzzling, because of their intermittent nature. Thus, headache and malaise might be present one day and gone the next. Nausea might then come on for a few hours, again leaving the patient feeling well. After alternating periods of minor symptoms and well-being, last-



ing for several days, the full-blown disease finally made its [3] appearance.

Of particular interest were certain symptoms that were present within the two weeks preceding the onset, but which apparently were independent of the actual disease. Such phenomena were noted in 36 instances; for example, S. had headache and a cold for two weeks, and H. had slight cough and occasional malaise for five days before onset. M. had coryza which cleared up two days before onset, K. had sore eyes and photophobia for a week, and N. had "coryza earlier in the week, which had practically subsided at onset." C. had been nervous and restless for four days, and J. had had a cough for two weeks before onset. In general, these "pre-onset" symptoms were in the nature of mild upper respiratory tract disturbances of from one to two weeks' duration, usually improving or well at the time of definite onset of the influenza.

*Physical Examination.*—Although evidence of gross lesions is absent in uncomplicated cases, the physical findings are none the less clean-cut and typical. The general appearance is most striking. In well-marked cases, there is an intense, dusky, reddish-plum-colored erythema of the face, lips and upper chest, which usually fades off abruptly at the level of the breast, but may extend over the entire chest and back, and occasionally involves the arms and legs. The entire facies has a remarkable suffused look, not unlike that seen in polycythemia vera. It is, however, quite different from true cyanosis, and studies of the oxygen-combining capacity and content of the blood in these patients gave normal results. The color blots out on pressure, returning instantly. In milder cases this tint is at times less striking, but it was present to some degree in practically all, and even where not obvious, a faint purplish erythema could be demonstrated by pressure. The peculiar dusky appearance of the face often persisted for weeks into convalescence, quite independent of transient flushing on exertion, which accentuated the underlying hue. In seven cases a fine, branny desquamation was noted over face and upper chest. Conjunctivitis was often very marked, with lachrymation and photophobia.

- [3] Early in the course of the epidemic we noticed an unusual bright red appearance of the throat in most of the patients, and more careful study of subsequent cases showed this to have striking and constant features. The changes in the mouth usually become full-blown during the first twenty-four hours of the disease. The most striking feature is a bright vermilion or scarlet injection of the pharynx, tonsils, pillars and soft palate. In many cases, this erythema extends over the entire mouth, and can be exquisitely demonstrated by pressure on the mucosa of the cheek with a spatula. In the
- [4] most marked cases, the entire mouth cavity has a flaming appearance. On analysis, this redness is seen to be due to a diffuse hyperemia of the mucous membrane, together with an injection of minute blood vessels on the pharynx and pillars, but especially on the soft palate. There is a line of demarcation at the hard palate, which is relatively free. In some cases, especially the mild ones, these changes are less marked, being confined to the soft palate and pillars. There is extreme swelling of the lymphoid tissue of the posterior pharyngeal wall, which gives it a remarkable corrugated appearance. These changes are clearly in the nature of an erythema, and there is never any localized exudate (Fig. 1).

The tongue is usually coated, but if clean is bright red like the buccal mucosa.

In from one-half to two-thirds of the cases at onset, one to three or four, or even more, dark, crimson spots were seen on the mucosa of the inside of the cheek (Fig. 2). They were occasionally present on the gums, soft palate, mucous border of the lips, or on the uvula. These spots vary from a minute pin-point up to one millimeter in diameter, and may be arranged in one or more clusters. The dark cherry color and sharp margin characterize them and seem to indicate that they are of hemorrhagic origin. The individual spots fade rapidly, disappearing without trace in from one to two days. They may reappear in repeated crops in the same individual, and are seen in convalescence in most of the cases. About 94 per cent of our patients in whom they were systematically looked for showed them at some time during the course of the disease.





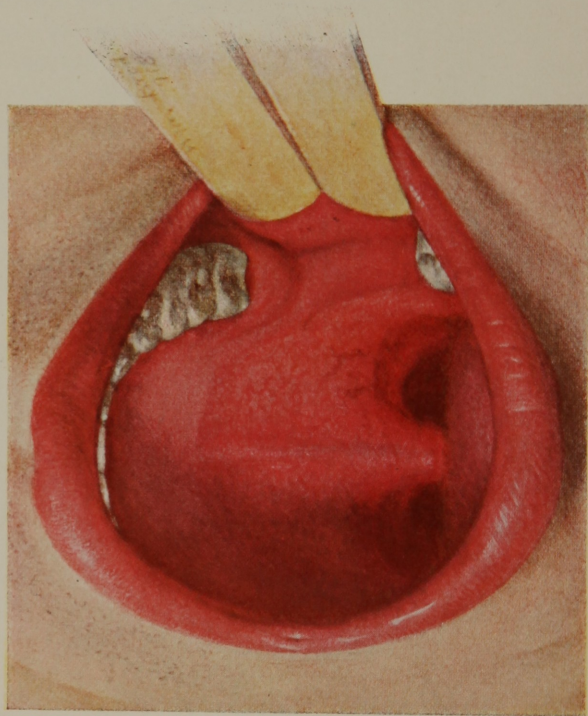


FIG. 1.





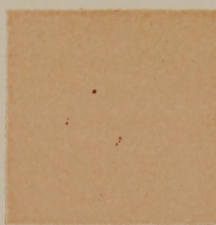
1



2



3



4

FIG 2.





Inasmuch as we had never observed such spots before, and [4] were unable to find any account of them in the literature, it appeared at first as if they might be specific of influenza as Koplik's spots are specific of measles. After the epidemic, however, it was possible to examine several hundred mouths of individuals who had had no symptoms of influenza, and in them also these spots were frequently present. In 303 examinations of 55 controls made daily over a period of one to nine days, the spots were seen 110 times, or in 36.6 per cent. They were seen at some time in 84.2 per cent of 38 controls examined daily over a period of a week or more. It was striking, however, that the spots were usually much smaller and less bright than in the influenza patients. Although they are obvious and often picturesque in the latter, they are frequently so insignificant in the controls that they are found only on careful search. Possibly the hyperemia of the mouth in influenza presents a specially favorable condition for their development. Their exact cause is uncertain; they may be due to slight trauma to the mucosa of the mouth. So that although these spots are not a specific lesion, their presence in typical form may have a certain degree of clinical specificity.

Another striking feature in the appearance of the mouth was a swelling of the minute nodules normally present on the soft palate. They were often extremely prominent, appearing as white or gray glistening, rounded bodies, varying in size from 1 to 3 millimeters in diameter. They were usually abundant, the entire soft palate being thickly seeded with them, and they stood out sharply against the surrounding hyperemia.

In summary, then, the mouth presents a very striking picture, which seems distinctly characteristic. Although, most writers have noted that the throat is injected, the observation by Tigri,<sup>2</sup> in 1867, now lost in obscurity, is the only one we have found which describes a typical enanthem. Tigri noted the peculiar injection of the soft palate, and likened it to the enanthem of measles.

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<sup>2</sup> Tigri: *Omodei annali di medicina*, Milan, 1867, CCII, 677.

- [4] The general appearance of the mouth may remain full-blown for about a week. The erythema then fades, usually leaving a striking capillary injection of the soft palate and pillars. In some cases, the redness of the entire mouth persisted for several weeks into convalescence.

Herpes was noted in nine per cent of the cases. In a few, it was present at onset, but might appear at any time during the active stage of the disease. It was no more frequent in the pneumonias than in the uncomplicated cases. There are no striking cardiovascular features; the pulse is usually only slightly accelerated, and the blood pressure tends to be subnormal. Abdominal examination is essentially negative. The spleen was felt in only three cases. Unless complication sets in, the lungs are clear, although a few transient crackles could at times be heard over the lower lobes at the beginning of the examination. Minor skin rashes were noted in 10 cases. A few erythematous papules on the chest and shoulders or a few small petechiæ were seen. Three patients had transient urticarial eruptions, and one a generalized morbilliform rash. In general, apart from the erythema, the skin changes are insignificant.

*Course of the Disease.*—Once fully established, the disease picture was remarkably constant. The fever usually continued high for from three to eight or nine days, with morning drops, the constitutional symptoms persisting until the temperature began to fall. At this time, particular discomfort, such as headache, backache, nausea, etc., gradually or suddenly disappeared, giving place to a profound feeling of collapse or exhaustion. The tight, racking cough often increased after the first day, with the production of more or less whitish, yellowish or greenish mucoid sputum, which in some cases persisted for weeks into convalescence. This is a regular feature of the disease, but other respiratory tract involvements must be regarded as complications. Some of the cases ran their whole course without cough, sputum or respiratory symptoms. Epistaxis was noted in 10 per cent of the patients. It occurred at onset, or at any time during the active stage, and in a few cases there were repeated epistaxes. This bleeding is doubtless associated with the



hyperemic condition of the nasal mucosa. Nearly all the [4] more severe cases had marked anorexia or nausea. The feeding problem became very difficult, and even fluid was refused. Stubborn constipation was the rule, although a [5] few patients had brief attacks of diarrhea. In no other disease does one see such constant lack of cheer in the patients' faces. Nothing satisfies them, they are extremely unhappy and gloomy, and seem to feel that things can never be normal or comfortable again. Pathological depressions were, however, strikingly absent in our cases.

*Convalescence.*—The classical post-influenzal asthenia described in previous epidemics was noted in these cases. Profound prostration persisted for weeks into convalescence. The patients for the most part feel fairly comfortable while lying flat in bed, but the slightest exertion is followed without warning by exhaustion, a feeling of collapse, sweating and palpitation. Apart from actual physical weakness, which is marked, they complain of an intensely disagreeable sensation, which may be best characterized as an extreme lack of well-being, rather than any positive pain or discomfort. This state of affairs usually persisted as long as the patients were under observation—about three or four weeks. Physical examination during convalescence is essentially negative. Tachycardia and sinus arrhythmias or extrasystoles are common, and in many cases the racking cough, with more or less mucoid or mucopurulent sputum, persists. Anorexia, headache and insomnia were frequent complaints and loss of weight up to 20 pounds was not uncommon.

*Mild, Abortive and Atypical Cases.*—These were of particular interest from an epidemiological and diagnostic standpoint. During the course of the epidemic about 20 cases were observed with such slight symptoms and signs that the presence of any definite disease was doubted. It was only at the end of about a week, when typical prostration appeared, that the diagnosis was made certain. Many patients did not apply for medical aid until this period of the disease, presenting as cases of tachycardia, insomnia or general breakdown. They furnished the key to a still larger group of very mild or abortive cases, which indicate clearly

- [5] that the total number of individuals affected is much greater than the number of manifest cases. In some of these individuals with practically no symptoms, the diagnosis was clinched by the typical appearance of the throat or by an extreme leucopenia.

Of the patients admitted to the wards, 30 ran an afebrile course, although there was usually some abnormality of the temperature curve. These were by no means the mildest cases; on the contrary, many who came down with sharp reactions recovered more promptly and were less prostrated.

#### LABORATORY EXAMINATIONS

*Urine.*—In the severer cases, a febrile albuminuria was present, usually clearing up promptly after free intake of water. No permanent renal disturbance was noted. The patients with pneumonia showed large amounts of albumin and casts.

*Blood Pressure.*—The blood pressure was either normal or low. Low readings were especially frequent in the very asthenic cases. Systolic pressures of 80 to 100 mm. Hg., and diastolic pressures as low as 50 were common. In convalescence, the pressures were essentially normal.

*Leucocytes.*—Leucopenia was the rule during the active stage of the disease. The average counts on the first or second day were about 4000 to 5000, but they varied from 2000 up to normal numbers in different cases. The low count persisted into convalescence, usually returning to normal during the third or fourth week. In some cases the normal mark was overshot, the count rising to 12,000 to 15,000—occasionally even higher. Differential counts during the stage of leucopenia usually show an absolute decrease of polymorphonuclears, with relative lymphocytosis. In some cases, the lymphocytes were absolutely decreased as well. It was of interest that many mild cases had extremely low counts, and that the leucocyte curves seemed unaltered by the occurrence of complicating bronchopneumonia.



## TEMPERATURE CURVES

Temperature readings were taken every two hours throughout the acute stage. In Table II is summarized the day of

TABLE II

THE DURATION OF THE FEVER ACCORDING TO THE DAY OF  
DEFERVESCENCE, AND THE NUMBER OF CASES

Temperature became normal on—

Day of Disease	in	Number of Cases
1 .....		0
2 .....		0
3 .....		7
4 .....		15
5 .....		25
6 .....		24
7 .....		44
8 .....		28
9 .....		22
10 .....		6
11 .....		4
12 .....		1 <sup>3</sup>

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<sup>3</sup> Bronchopneumonia?

In 30 cases there was no fever during the hospital stay.

the disease on which the temperature became normal. It is apparent that this is not a three-day fever. Even in uncomplicated cases, the pyrexia usually lasts from five to nine days. From a study of complete temperature curves obtained in cases developing in the wards, it was possible to determine the details of the entire course of the fever. The following general statements may be made:

1. The temperature rises gradually at onset, rarely reaching its height in less than 24 hours.
2. Fever continues for a variable period, falling gradually in about one-half the cases, and suddenly (in 24-36 hours) in the remainder.
3. There is rarely a steady fastigium, the morning temperature usually being from one to three degrees lower than the evening reading.

[6] 4. After falling, the temperature may remain normal, it may be subnormal for several days, or there may be slight post-febrile rises.

5. Secondary rise of fever usually indicates a complication, but such rise may occur in uncomplicated cases.

6. An occasional chart may show an entirely bizarre, non-uniform curve.

7. Some charts show only slight elevations throughout the course.

8. The pulse is usually relatively slow, but follows the temperature curve in a general way.

It appears, therefore, that while the temperature curves vary in character, the fever is one of distinctly determinate duration. In 95 per cent of the cases the temperature reached normal by the ninth day, and in no uncomplicated case did it persist beyond the eleventh day. Some of the main features of the fever are shown in the appended charts.

#### COMPLICATIONS

Apart from the pneumonias, which occurred in 41, or 15.3 per cent of the cases, complications were few. Mild sinus infections occurred in two cases, catarrhal otitis media in six, while one patient developed an acute mastoiditis requiring operation. Laryngitis giving frank symptoms occurred three times.

A group of 19 patients was of particular interest. They developed localized patches of fine, crackling rales, with some impurity of breath sounds over one or both lobes. These signs usually appeared at the height of the disease and persisted for a few days to several weeks. A beginning pneumonia was naturally suspected, but in no case was there bloody sputum, respiratory symptoms, or any unusual rise of temperature. The normal course of the disease seemed unaltered. X-rays made in several of these cases showed no localized shadow.

#### EPIDEMIOLOGICAL OBSERVATIONS

Despite the striking general facts in regard to the gross spread of the disease, the details of contagion and infection



are quite obscure. We desire to put on record certain ob- [6]  
servations which seem of interest, without attempting to draw  
any definite conclusions.

The disease is contagious during the incubation period. E. visited his sister who was at a country place where no influenza had appeared. He was there for a few hours in the morning. On his arrival in Baltimore six hours later, symptoms appeared. He had a severe type of the disease, with secondary pneumonia of which he died on the eighth day. Two days after contact the sister developed a severe case of influenza. Family H. were in the country with no influenza in the vicinity. Mrs. X. and her son came to visit them. A day or so later, the boy developed the disease. H., who is a physician, sent mother and boy away at the onset of symptoms, but three days later his own three children developed severe attacks. These observations are also in harmony with the generally accepted idea that the incubation period is about two days.

Medical student B. came to Baltimore with the disease full-blown. His room-mate slept in the same bed with him for two nights, but did not develop influenza. Most of the nurses are quartered two in a room. Among 150 of them who developed influenza, there were only 12 pairs of room-mates. Except in the case of three pairs, each of the two came down within two days of the other. This perhaps indicates that infection took place mainly before symptoms were well developed, when the nurses were in general contact in the assembly rooms and dining hall. General use of gauze face masks in the wards did not seem to alter the course of the epidemic. If these masks are protective, infection from early unisolated cases must be assumed.

Only eight of the patients in the general public wards developed influenza, although 40 per cent of the attendants were affected; and numerous individuals did not contract influenza until they had been constantly exposed for as long as two weeks.

These observations are of interest in so far as they confirm facts noted in previous epidemics, and indicate our total lack of insight into the details of the mode of infection and

- [6] spread of the disease, apart from the gross fact of its extreme contagiousness.

### ETIOLOGY

- A consideration of the etiology of influenza must include a discussion of two questions. Is the influenza bacillus the cause of the disease, and if not, what is the etiological agent? The main evidence in favor of the Pfeiffer bacillus' being the cause of influenza is the observation that in certain localities it has been isolated from the respiratory passages in a large percentage of the cases. Against its etiological nature, several facts may be noted: Apart from the presence of the organism, no definite relation to the uncomplicated disease by isolation from a specific lesion, or development of immunity reaction, has been proved. Neither experimentally in animal or in man has influenza or a condition simulating it been produced by inoculation with cultures of the influenza bacillus. The influenza bacillus is present in interepidemic times in the nasopharynx of normal persons, and in a large percentage of acute and chronic respiratory infections. Luetscher, for example, in 603 sputum cultures, isolated the influenza bacillus in pure culture from 28.5 per cent of cases of non-tuberculous infection. The organism is essentially symbiotic with other bacteria, both *in vivo* and *in vitro*. It is well known that it grows much better in the presence of other bacteria, such as staphylococci, giving rise to so-called giant colonies. In isolating pneumococcus from sputum by mouse inoculation, the influenza bacillus commonly comes through into the animal's blood with the pneumococcus, while other organisms remain localized in the peritoneum. Sputum cultures from cases of lobar pneumonia may yield *B. influenzae* in pure or almost pure culture, where the lung puncture shows only pneumococcus, indicating the tendency
- [7] of the organism to press in wherever other bacteria are present. The influenza bacillus has been found in tonsils, inflamed and normal, in pleurisy, in sinus and middle ear infections, in the entire respiratory tract from nose to alveoli, in bronchiectases, in the urinary tract, in the meninges, and in association with tuberculosis, diphtheria, measles and



scarlet fever. In these conditions, the rôle of the influenza [7] bacillus, while superficially prominent, is clearly not fundamental.

Bacteriological studies, made in our cases by Dr. Howard, which are reported in detail elsewhere, did not bring evidence that the bacillus of Pfeiffer is the cause of epidemic influenza. Blood cultures made at onset in the acute cases were uniformly negative, and it was only in the terminal stage of the complicating pneumonias that organisms appeared in the blood. Pneumococcus or streptococcus was isolated in a few instances, but no influenza bacilli. Naso-pharyngeal swabs made at onset showed the usual mouth flora. Gram-negative bacilli were seen in smears in some of the cases, but only once as the predominating organism. In three instances of post-influenzal pneumonia, the Pfeiffer bacillus predominated in the sputum culture, but in most cases the pneumococcus, green streptococcus and other organisms were mainly present.

Similar bacteriological findings which are now being reported by other observers cast doubt on the rôle of the Pfeiffer bacillus as the primary cause of uncomplicated epidemic influenza; it is probable that the actual virus is as yet unidentified. It is of interest, however, to point out some striking analogies between this disease and certain of the acute exanthemata, especially measles. They are both extremely contagious. They both tend to break out in epidemic form from time to time, but sporadic cases persist between epidemics. Each has an incubation period of strikingly constant length and a febrile reaction of determinate duration. They both have characteristic leucocytic changes. The uncomplicated cases all show striking absence of gross lesions. In both diseases these are hyperemic phenomena of the skin and throat, and a remarkable tendency to complications, especially in the respiratory tract. It should, however, be strongly emphasized that there is no evidence of any actual relationship between these two diseases.

## CONCLUSIONS

[7] The observations herewith presented may be summarized as follows:

1. Epidemic influenza in 1918 is clinically identical with the disease as seen in previous pandemics.

2. It is not primarily a local disease of the respiratory tract.

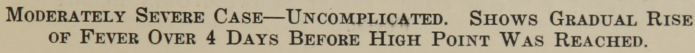
3. It presents a definite and characteristic clinical picture quite apart from the pulmonary complications.

4. The main features of the uncomplicated disease are a constant set of symptoms, characteristic erythema and appearance of the mouth, fever of determinate duration, and leucopenia.

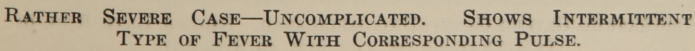
5. Proof is lacking that the Pfeiffer bacillus is the primary cause of uncomplicated influenza.



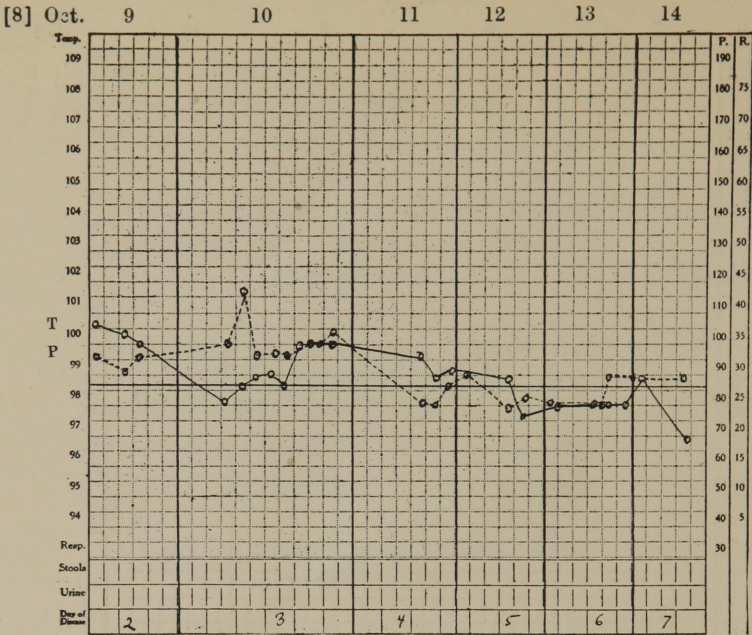
Oct. 6 7 8 9 10 [7]



Oct. 8	9	10	11
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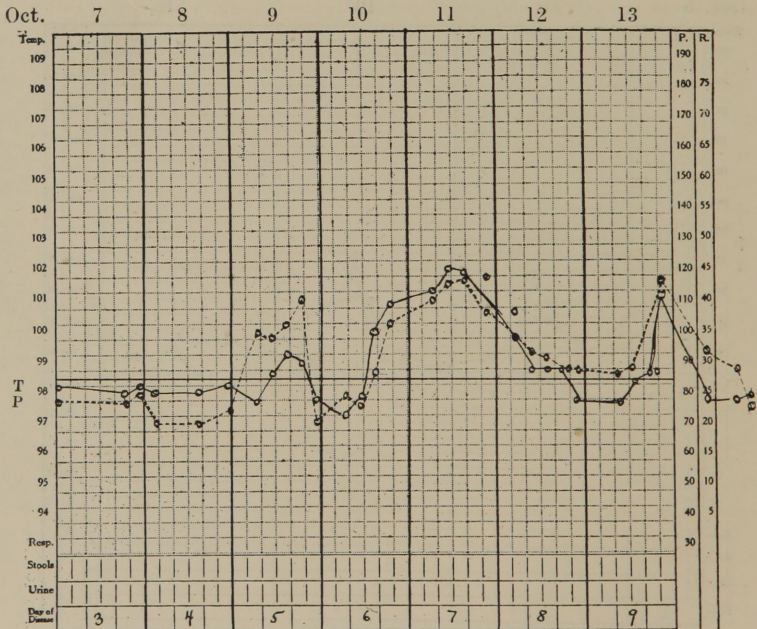


# CHART IV



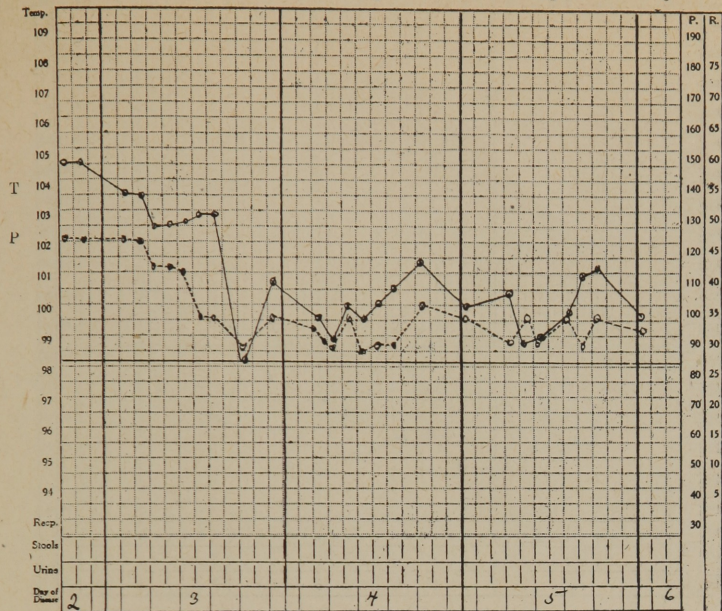
AN EXTREMELY SEVERE CASE. CHART SHOWING ONLY SLIGHT FEVER.

# CHART V

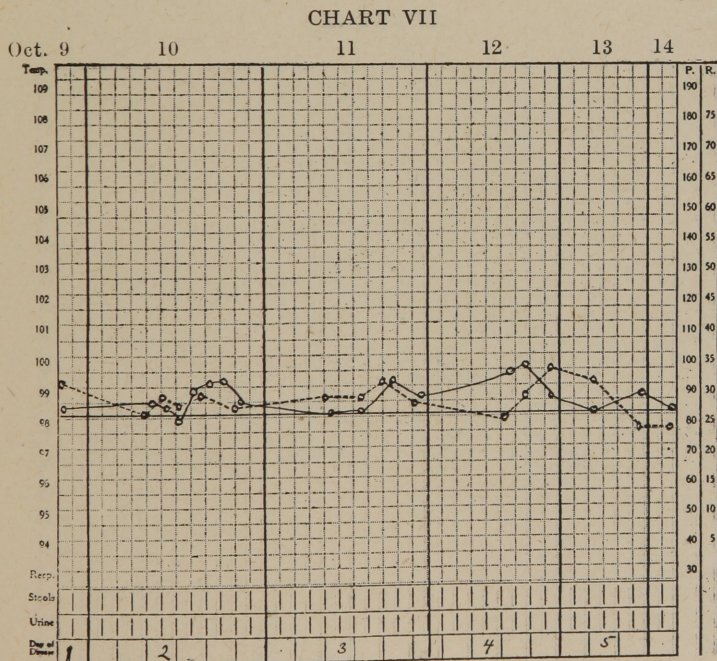


MODERATELY SEVERE CASE—UNCOMPLICATED. SHOWS LATE RISE OF TEMPERATURE ON THE 6TH TO 8TH DAY.





A FULMINATING CASE. CHART SHOWS VERY HIGH FEVER.



MODERATELY SEVERE CASE SHOWING VERY SLIGHT FEVER.



# CHART VIII

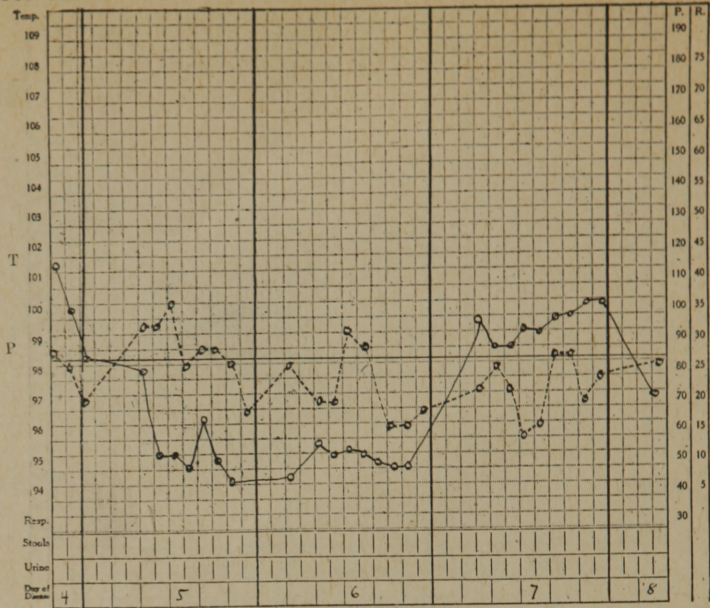
[9] Oct. 18

19

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21

22



MODERATELY SEVERE CASE—UNCOMPLICATED. SHOWS FEVER FOLLOWED BY SUBNORMAL TEMPERATURE.

# CHART IX

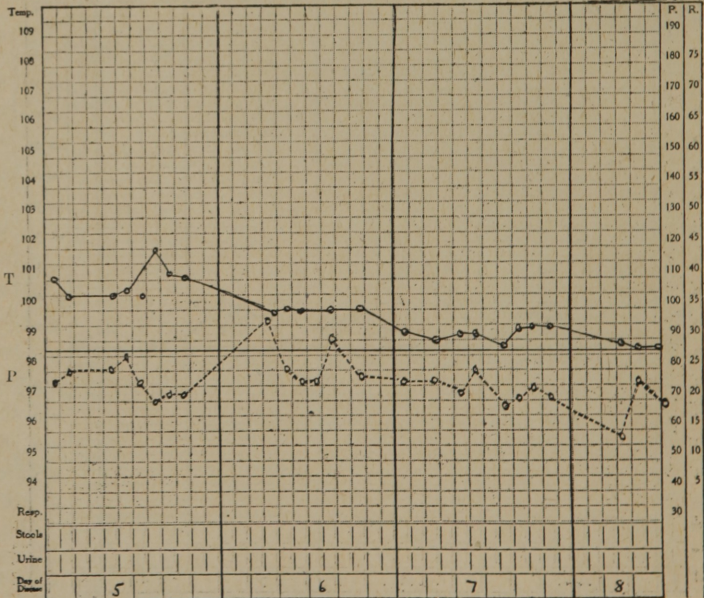
Oct.

3

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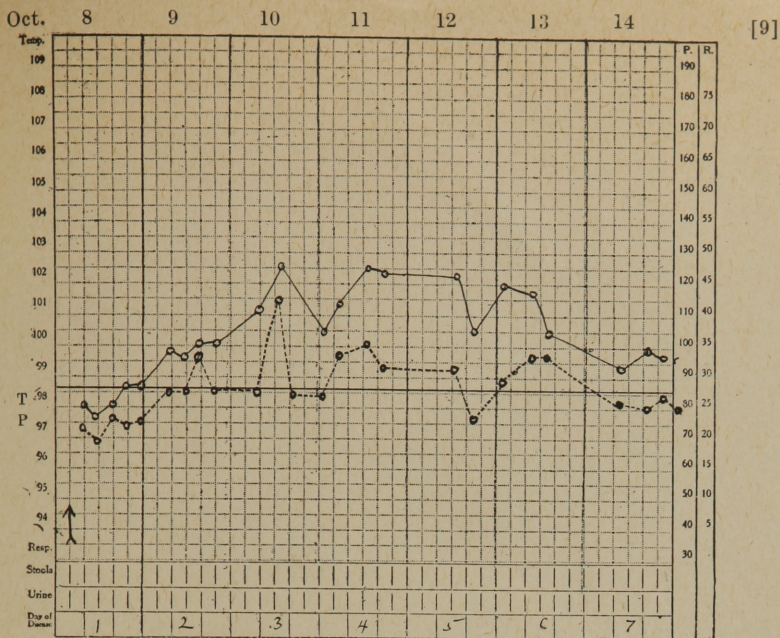
6



VERY SEVERE CASE—UNCOMPLICATED. SHOWS CHART FROM 5TH-8TH DAY. GRADUAL FALL OF TEMPERATURE—RELATIVE BRADYCARDIA—ABSOLUTE BRADYCARDIA IN CONVALESCENCE.

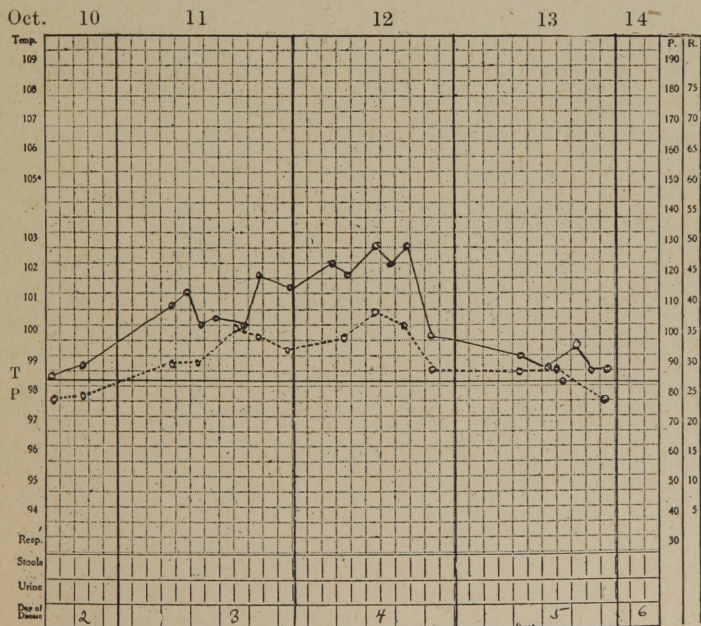


# CHART X



A PATIENT WHO CONTRACTED INFLUENZA IN THE WARD. SYMPTOMS BEGAN AT ↑. SHOWS GRADUAL RISE OF TEMPERATURE.

# CHART XI



A FULMINATING CASE WITH INTENSE SYMPTOMS ESPECIALLY HEAD-ACHE. CHART SHOWS GRADUAL RISE OF FEVER. SUDDEN FALL OF FEVER WITH PROMPT RELIEF OF SYMPTOMS ON 5TH DAY—FOLLOWED BY PROSTRATION.







